REMARKS

I. CLAIM STATUS

Claims 1-5, 7, 11, 13-17 and 19 were pending when last examined.

Claims 11, 13-17 and 19 are withdrawn from consideration as non-elected subject matter.

Claims 1-5 and 7 were examined and are rejected.

II. PRIORITY UNDER 35 USC § 119

The Examiner has not acknowledged the claim for foreign priority by checking the appropriate boxes in item 12 of the Office Action Summary sheet. However, a claim for foreign priority is indicated in PAIR. Moreover, Applicants note that a certified copy of the priority document was received by the Office on September 28, 2005. See PAIR. Accordingly, the Examiner is respectfully requested to acknowledge the claim for foreign priority by checking the appropriate boxes in the next action.

III. REJECTION UNDER 35 USC § 102

In item 4 on pages 3 and 4 of the Office Action, claims 1-5 and 7 are rejected under 35 USC § 102(b) as being anticipated by Kato et al. (WO 04/08001, April 1994, US equivalent 5,597,713, January 1997).

Applicants respectfully traverse this rejection.

The claimed invention teaches a linear mRNA/cDNA heteroduplex having a first linear end comprising "mRNA/cDNA" and a second linear end comprising "DNA/DNA" (double-stranded DNA primer). See step (ii) of claim 1; see also page 13, line 26 to page 14, line 3. The first end (mRNA/cDNA) and the second end (DNA/DNA) of the linear heteroduplex are then joined by T4 RNA ligase to form a circular mRNA/cDNA heteroduplex. See step (iii) of claim 1; see also page 14, lines 9-24.

In contrast, the linear mRNA/cDNA heteroduplex of Kato et al. comprises a first end of "DNA/DNA" and a second end of "DNA/DNA" (double-stranded DNA primer). See Fig. 1 and 2 of Kato et al. Specifically, the double-stranded DNA primer is annealed to a DNA/RNA

chimeric oligonucleotide-ligated mRNA. The first strand cDNA is synthesized from the primer to form the mRNA/cDNA heteroduplex. Subsequently, the first end (DNA/DNA) and the second end (DNA/DNA) of the heteroduplex are ligated at a digestion site of the DNA vector by T4 DNA ligase to form a circular vector containing the mRNA/cDNA heteroduplex.

Accordingly, the ligation partners of this invention are "mRNA/cDNA" and "DNA/DNA" while the ligation partners of Kato et al. are "DNA/DNA" and "DNA/DNA." Furthermore, the Examiner's position that Kato et al. teaches "circularizing the mRNA/cDNA using T4 RNA ligase to form a circular mRNA/cDNA heteroduplex..." is misplaced. Specifically, Kato et al. uses T4 DNA ligase rather than T4 RNA ligase, i.e., Kato et al. ligates DNA and DNA using the T4 DNA ligase. The T4 RNA ligase of Kato et al. is used for ligating the DNA-RNA chimeric oligonucleotide with mRNA, but circularizing the heteroduplex is performed with T4 DNA ligase. See Fig. 1 of Kato et al. Even though Kato et al. does not explicitly describe the use of T4 DNA ligase for circularation, such use is common knowledge in the art for ligating DNA and DNA. Therefore, a person having ordinary skill in the art would have recognized that T4 DNA ligase was utilized for such purpose. In fact, a T4 RNA ligase would be ineffective to ligate two strands of DNA. Accordingly, Kato et al. fails to teach the use of T4 RNA ligase for joining "mRNA/cDNA" and "DNA/DNA" ligation partners into a heteroduplex. Further, Kato et al. fails to teach that the first linear end of the heteroduplex is mRNA/cDNA and the second linear end is DNA/DNA.

In light of the above, it is clear that Kato et al. fails to teach all the limitations of the claimed invention. Accordingly, this rejection is overcome and should be withdrawn.

IV. REJECTION UNDER 35 USC § 103

In items 6 on pages 4-7 of the Office Action, claims 1-5 and 7 are rejected under 35 USC § 103(a) as being unpatentable over Chenchik et al. (of record) in view of Brennan et al. (Methods in Enzymology, vol. 100, pages 38-52). Specifically, the Examiner contends that Chenchik et al. teaches the method of claim 1. The Examiner concedes that Chenchick et al. teaches a T4 DNA ligase rather than the T4 RNA ligase of the present invention. However, the Examiner contends that Brennan et al. provides a general teaching of T4 RNA ligase and that

Kato et al. supports the teachings of Brennan et al. by the use of T4 RNA ligase for the purposes of ligating DNA-RNA chimeric oligonucleotide to mRNA. See col. 3, lines 47-64. Therefore, the Examiner takes that position that it would have been obvious to a person having ordinary skill in the art to substitute T4 RNA as taught by Brennan et al. and Kato et al. in the place of T4 DNA ligase as taught in Chenchik et al. since an ordinary artisan has good reason to pursue all known options within his technical grasp known not to negatively alter such method.

Applicants respectfully traverse this rejection.

Chenchik et al. teaches a mRNA/cDNA heteroduplex having a first end comprising "DNA/DNA" (CapSwitch oligonucleotide (DNA) and Capswitch anchor (DNA)) and a second end comprising a double-stranded primer (DNA/DNA). Therefore, the heteroduplex of Chenchik et al. is similar to the heteroduplex of Kato et al. As described above, T4 DNA ligase is required for ligating such a heteroduplex to form a circular vector. Moreover, T4 RNA cannot be used to form such circular vector in such a heteroduplex.

Accordingly, the references fail to teach or suggest all the limitations of the claimed invention. Moreover, a person having ordinary skill in the art would not be motivated to use T4 RNA ligase on the heteroduplexes of Kato et al. or Chenchik et al. because such combination would be expected to be ineffective to form a circular vector.

Further, Brennan et al. shows only that T4 RNA ligase can join a single-stranded DNA with another single-stranded DNA by ligation. Brennan et al. fails to teach or suggest wherein T4 RNA is effective to ligate mRNA/cDNA together with double-stranded DNA. In fact, Applicants were first to discover the remarkable property that T4 RNA ligase can ligate the heteroduplex of the present invention to form a circular vector.

Therefore, the present invention is unexpectedly superior to the cited references because such method eliminates the need to use a DNA-RNA chimeric oligonucleotide as in Kato et al. and an anchor DNA as in Chenchik et al. Since none of the cited references teach or suggest such superior result, this rejection is overcome and should be withdrawn.

Finally, applicants note that "where a reference is relied on to support a rejection, whether or not in a minor capacity, that reference should be positively included in the statement of the rejction." See MPEP 706.02(k). On page 6 of the Office Action, the Examiner states,

> "[t]hus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to substitute T4 RNA ligase as taught by Brennan and Kato in place of the Tv DNA ligase in the synthesis method of Chenchik since the ordinary artisan has good reason to persue the known options within his or her technical grasp... In turn, because RNA ligase is known to ligate DNA oligoneucleotides, RNA oligonucleotides or chimeric oligonucleotides comprising RNA-DNA to mRNA as taught by Brennan and Kato, ..."

Applicants note that the Examiner has relied on Kato et al. in determining *prima facie* obviousness. Accordingly, since the statement of the rejection does not positively include the Kato et al. reference, this rejection is improper and should be withdrawn.

CONCLUSION

Therefore, in view of the forgoing remarks, it is submitted that the ground of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

Seishi KATO et al.

By: /William R. Schmidt, II/

Digitally signed by /William R. Schmidt, II/
DN: cn=/William R. Schmidt, II/, o=WLP, ou, email=bschmeltzwonderath.com, c=US
Date: 2009.09.08 12:34:35 -04'00'

William R. Schmidt, II
Registration No. 58,327
Attorney for Applicants

WRS/cg/vah
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
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